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# Long term remission with Sirolimus for a pediatric patient with an EBV-associated smooth muscle tumor after bone marrow transplantation

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## Introduction

- Epstein-Barr virus (EBV) is a ubiquitous human herpes virus associated with a broad range of malignancies due to its oncogenic potential.
- Immunocompromised patients, especially those after transplantation have a strong disposition to EBV infection and development of smooth muscle tumors (SMTs)
- Lee et al described two cases in 1995 and discovered the link between EBV and the development of SMTs
- EBV-associated smooth muscle tumors (EBV-SMT) are rare with an estimated incidence of 1%-5%
- The incidence of EBV-SMTs after hematopoietic stem cell transplantation is extremely rare and reported only in a few cases with the majority occurring in pediatric patients
- Clear risk factors have not been identified including the type of immunosuppressive drugs, solid versus hematopoietic transplant, or manifestations of PTLD
- Approximately 38% of transplant associated EBV-SMT and 40% of HIV-associated EBV-SMTs occur in children, and those related to immunodeficiency are rare and described in a few case reports

## Case Presentation

- A nine-year old female presented with acute onset abdominal pain, diarrhea, nausea, and vomiting.
- During her initial evaluations a CT scan of the abdomen and pelvis was obtained that showed numerous large heterogeneous masses in the liver
- Past medical history:
  - B-cell acute lymphoblastic leukemia (ALL)
  - Three years after treatment she had a relapse of her B-cell ALL and was treated with a matched allogeneic bone marrow transplantation using male umbilical cord stem cells and achieved complete remission
  - Treated with immunosuppressive regimen including Tacrolimus, Mycophenolate, and Prednisone.
- Biopsy revealed a mesenchymal neoplasm with myxofibroblastic proliferation consistent with a smooth muscle tumor.

## Clinical Course

- A panel of markers including CD3, CD20, kappa, and lambda was performed and was negative, excluding the possibility of post-transplant lymphoproliferative disease.
- Tissue involvement with EBV was demonstrated by PCR and immunostaining for LMP-1 confirming the diagnosis of an EBV-SMT.
- She was started on Sirolimus, 1 mg, Prednisone, and antiviral therapy.
- Due to the size and multitude of masses in the liver surgical resection was not pursued.
- Repeat CT scan of the abdomen 12 months after initiation of therapy with Sirolimus showed decreased size of the liver masses.
- At her current evaluation, she remains without tumor progression and stable without relapse.

## Pathology

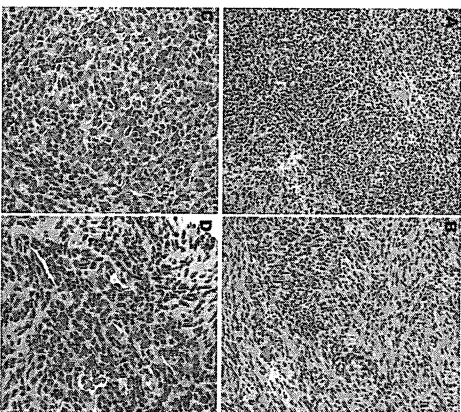


Figure 2: EBV-associated smooth muscle tumors morphologically resemble other smooth muscle tumors, being composed predominantly of hyperchromatic spindle cells predominantly in RNA.

## Discussion

- This case represents the one of the few reported pediatric cases of long-term therapeutic responses with Sirolimus for EBV-SMTs.
- Due to the low incidence and varied clinical presentation of EBV-SMTs, knowledge of effective therapies are limited.
- Current treatment strategies include surgical resection, alterations in immunosuppression, anti-viral medications, and chemotherapy.
- AKT pathway and the mammalian target of rapamycin (mTOR) pathway are the most notable EBV pathogenesis pathways
- The mTOR pathway performs a key role smooth muscle proliferation and activation of the Akt/mTOR signal pathways via nuclear staining was observed in majority of tumors in several case reports
- Several case reports have demonstrated remission with Sirolimus, an mTOR pathway inhibitor, in patients with EBV-SMTs.
- Research on clinical improvement and remission for pediatric patients with EBV-SMT is limited and this case report demonstrates the long-term remission and therapeutic implications of early detection and initiation of therapy with Sirolimus for EBV-SMTs.

## References

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